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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.

EXAMINER	
ART UNIT	PAPER NUMBER
	10

DATE MAILED:

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/484,331	Applicant(s) HARRINGTON ET AL.	
	Examiner Ram R Shukla	Art Unit 1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 September 2000* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *58-61* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *58-61* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. & 119(e).

Attachment(s)

15) ☐ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 6 .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other: .

DETAILED ACTION

Priority

1. Amendment filed 9-1-2000 has been entered.

Claim Rejections - 35 U.S.C. □ 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 58-61 remain rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, for reasons of record set forth in the previous office action.

Response to Applicants' Arguments:

Applicant's arguments filed 9-1-2000 have been fully considered but they are not persuasive.

In the previous office action the two main issue were: lack of any knowledge of the gene activated and lack of any clues as to what is the phenotype to be tested in the drug screening. Since these two issues are compounded by other issues discussed in the previous office action of 4-28-00 (see pages 4-7), an artisan would have required undue experimentation to practice the claimed invention.

In response, Applicants have argued that the claimed method can be practiced by measuring a change in any detectable phenotype and such a phenotype may be- RNA or protein from the activated gene or biological activity of the protein, whether the activated gene is a known gene or unknown gene or whether there is any known correlation between a gene and a disease. Applicants have argued that based on the specification and the knowledge in the prior art an artisan would be able to practice the claimed invention. Applicants have also brought up the issue of activation of various genes by the claimed method discussed in the office action of 09/276820, however, for this issue Applicants are referred to the response sent regarding said application.

First, Applicants argued that the step 2 of the method (culturing cells) is routine and that treating a cell with a test compound is also routine in the art. There is no contesting of this, rather the issue here is: that a key step in the process of selecting a molecular target for a drug discovery program involves a demonstration that altering the activity of the proposed target should affect the disease and the specification does not provide guidance as to how an artisan would be able to decide about this key step when there is no clue what gene has been activated by the claimed method. Applicants argument that the article of Caporale is for selecting a molecular target for a drug and not for discovering a drug is not persuasive because the article by Caporale discusses issues in drug discovery. Applicants reiterate that the issue in the instant case is drug screening, not target selection, in response Examiner reiterates that without knowing a target how will the screening be carried out? The issue therefore remains for screening of a compound, one has to know a screening assay? And Applicants' arguments do not address this issue. As noted in the previous office action, it is reiterated that when the expression of an unknown gene is activated and there is some change in the phenotype of a cell, in the absence of any clues as to what disease such a phenotype or activated gene is related to, how would a drug or compound be selected for screening.

Applicants argue that the phenotype could be a gene product or a biochemical activity, however, it is not clear how can an artisan screen for these phenotypes without knowing anything about them. For example, the activation of a gene causes increase in the activity of an enzyme, there is no way of knowing what enzyme has been increased, then, how would an artisan know what enzyme to assay for? Again regarding the assay conditions, one would realize that the enzyme activity screening, RNA expression analysis or any other biological activity screening would require an initial step of determining as to which enzyme or which class of enzyme is to be studied or what are the characteristics of a protein to assayed for, and without this information, how will any one decide which enzyme substrate or assay conditions to use for screening. It is noted that other issues regarding the assay of the activated protein were raised in the previous office action, such as inactivation of the protein during concentration of the culture medium due to the protein being a component of a multi-protein complex (see page 7), which would further complicate the steps 3 and 4 of the method and Applicants arguments do not address these issues.

Applicants argue that the problem regarding non-specific entry of a drug into a cell is specific to one mechanism and not to others (as reviewed by Czerwinski et al, PNAS), however, it is not true because uptake of a drug could be an issue in any case based on the intracellular site of action of the drug and the chemical nature of the drug. Applicants argue that the cited example does not apply in most instances of drug development and that this would be the case only with a subset of genes. In response, it is noted that if it applies to some cases and the claimed invention is not limited to a drug development targeted to a certain gene, this remains an enablement issue.

Next, Applicants argue that even if a protein is not full length, it can be used in screening because it may retain one or more activities present in the full length protein or it may have a motif that may bind to a ligand or a drug. Again, how would an artisan know what is the activity of a truncated protein without any idea of what the activated gene is or what is the activity of the full length protein. Applicants have argued that truncated proteins are also capable of generating a detectable phenotype, however, they do not provide any example to support their assertion.

Next, Applicants argue that even when screening highly characterized targets, it is often difficult or impossible to predict which compounds will be active drugs and accordingly thousands of diverse compounds are screened. In response it is noted that in such a case there will be a starting point where one knows the target of a drug or compound and will choose a library of drugs or compounds that would have certain characteristic(s) based on the target. However, in the instant case, when the target is not known how would a particular compound or a library of compounds be selected for screening. It is Examiner's understanding that the compounds in a library would not be grouped together without any similarities or considerations, rather they would have certain similar characteristic that would allow them to be categorized in a certain group. And ordinarily, the relationship of such a similarity or characteristic to a certain biological activity or function would make them a candidate in a screening assay. In the instant method, there is no way of making this determination in the absence of any clue about the gene being activated.

In conclusion, Applicants arguments do not address the issues raised in the previous office action and therefore, the specification is not enabling for the claimed invention because

the specification does not provide sufficient guidance, evidence or exemplification so that an artisan of skill would have been able to make and use the claimed invention without undue experimentation.

4. No claim is allowed.

5. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ram R. Shukla whose telephone number is (703) 305-1677. The examiner can normally be reached on Monday through Friday from 7:30 am to 4:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Karen Hauda, can be reached on (703) 305-6608. The fax phone number for this Group is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 305-0196.

Ram R. Shukla, Ph.D.

Scott D. Priebe

SCOTT D. PRIEBE, PH.
PRIMARY EXAMINER